

Remarks

After entry of the amendment, claims 12-35 are pending.

Claims 1-11 have been canceled without prejudice.

Claims 12-35 are supported by the originally filed claims and the specification at, for example, page 5, lines 4-17; page 10, lines 3-9

No issues of new matter should arise and entry of the amendment is respectfully requested.

Rejection under 37 CFR § 112, Second Paragraph

Claim 5 is rejected under 37 CFR § 112, second paragraph, as being indefinite.

Applicant respectfully traverses the rejection and respectfully submits that the term "severe" is not indefinite. One skilled in the art of movement disorders would appreciate what the term "severe" means and would understand that "severe" means more than moderate in degree. The website for the Worldwide Education and Awareness for Movement Disorders at www.wemove.org (a copy of which is submitted in the IDS concurrently herewith) provides a "Tremor Scale" for the symptomatic complaint of tremor in any part of the body. The Tremor Scale, which is reproduced below for the Examiner's convenience, has a category for "severe" tremors, indicating that "severe" is term well known to one skilled in the art.

	Tremor	Symptom
0	absent	no tremor or writing impairment
1	slight and infrequently present	mild tremor, writing, and drawing of spiral minimally impaired
2	moderate; bothersome to most patients	writing and drawing of spiral moderately impaired
3	severe tremor	writing and drawing severely impaired; interferes with many activities such as drinking liquids
4	marked tremor	interferes with most activities

Additionally, Racette et al, *Stereotact Funct Neurosurg.*, 75(4):155-9 (2000) and Murata et al, *J. Neurosurg.*, 99(4):708-15 (2003) (a copy of each of which is submitted in the IDS concurrently herewith) provide evidence that one skilled in the art would recognize that the term

“severe” is routinely used in combination with the phrase “essential tremor” to describe the severe form of the disorder.

Because “severe,” when used to describe tremors, is a term of art, one of ordinary skill in the art would be reasonably apprised of the scope of the invention. In view thereof, Applicant respectfully requests that the rejection under 35 USC § 112 be withdrawn.

First Rejection under 35 USC § 103

Claims 1-3 and 5-10 are rejected under 35 USC § 103 as being obvious over WO 99/33465 ('465 application) in view of Moore et al., *Journal of Physiology*, 529(1):273-281 (2000) (Moore).

Applicant respectfully traverses the rejection and respectfully submits that the '465 application in view of Moore does not disclose or suggest the claimed invention. Because the '465 application is in Japanese, Applicant will address this rejection with respect to US Patent No. 6,342,515 (hereafter the '515 patent), which claims priority under § 371 to the '465 application. It is Applicant's assumption that the disclosure in the '465 application is the same as the disclosure in the '515 patent.

The '515 patent teaches the use of zonisamide to treat neurodegenerative diseases, such as Parkinson's disease. At column 1, lines 23-28 (Emphasis Added), the '515 patent states:

With developing into an aging society, the number of patients suffering from neurodegenerative diseases such as Parkinson's disease is increasing. Parkinson's disease is a progressive and tragic disease by which **coordinated movement of patient is disturbed**, and the **movement of patient becomes slow** with the lapse of time, and finally, **rigidity or tremor** of arms and legs develop.

While the '515 patent teaches the use of zonisamide to treat Parkinson's disease, the '515 patent identifies numerous symptoms associated with Parkinson's disease, but does not disclose or suggest what symptoms of Parkinson's disease zonisamide is useful in treating. There is no disclosure or suggestion that zonisamide is useful in treating every symptom of Parkinson's disease. There is no disclosure or suggestion that zonisamide is useful in treating tremors associated with Parkinson's disease, and there is no disclosure or suggestion as to what types of tremors are associated with Parkinson's disease.

Moore teaches that postural and resting tremors are often associated with Parkinson's disease. Moore does not disclose or suggest that any other types of tremors are associated with Parkinson's disease. Moore does not disclose or suggest zonisamide; does not disclose or suggest that zonisamide can be used to treat any types of tremors; and does not disclose or suggest that zonisamide can be used to treat Parkinson's disease or any types of tremors associated with Parkinson's disease.

With respect to original claim 2, Moore teaches that postural tremors are associated with Parkinson's disease and the '515 patent teaches zonisamide for treating Parkinson's disease; however, neither Moore nor the '515 patent disclose or suggest the use of zonisamide to treat postural tremors (regardless of whether or not they are associated with Parkinson's disease). The references are silent on the use of zonisamide to treat postural tremors, and the PTO has not provided any reasonable expectation that zonisamide could successfully be used to treat postural tremors that are associated with Parkinson's disease. The PTO has not established any link or relationship between zonisamide and the postural tremors associated with Parkinson's disease. In view thereof, original claim 2 is unobvious over the combination of cited references.

With respect to original claims 3 and 5-10, the '515 patent and Moore do not disclose or suggest any relationship between Parkinson's disease and one or more of the claimed tremors (i.e., essential tremors, severe essential tremors, drug-induced or toxic tremors, cerebellar tremors, primary orthostatic tremors, dystonic tremors, and neuropathic tremors). Because the PTO has not established any relationship between Parkinson's disease and these types of tremors, and because the '515 patent and Moore do not disclose or suggest the use of zonisamide to treat essential tremors, severe essential tremors, drug-induced or toxic tremors, cerebellar tremors, primary orthostatic tremors, dystonic tremors, or neuropathic tremors, original claims 3 and 5-10 are unobvious over the combination of cited references.

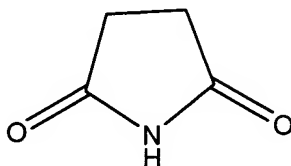
Applicant respectfully submits that the '515 patent in view of Moore does not render the pending claims obvious, and respectfully requests that the rejection under 35 USC § 103 be withdrawn.

Second Rejection under 35 USC § 103

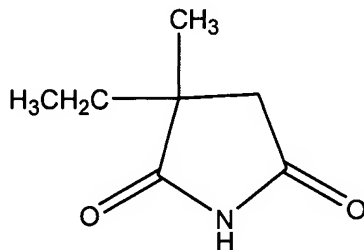
Claims 1-11 are rejected under 35 USC § 103 as being obvious over US Patent No. 4,981,867 (the '867 patent) in view of Kito et al., *Seizure*, 5(2):115-119 (1996) (Kito).

Applicant respectfully traverses the rejection and respectfully submits that the '867 patent in view of Kito does not disclose or suggest the claimed invention.

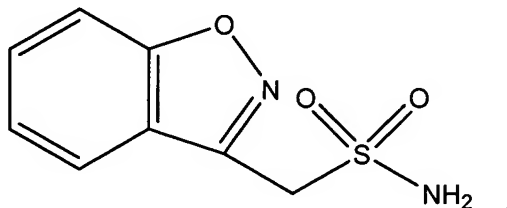
The '867 patent teaches that succinimides, especially ethosuximide, are compounds that depress the transient calcium current in thalamic neurons in Wistar rats (column 3, lines 1-13; column 5, lines 42-47) and are effective for treating certain types of tremors (column 5, lines 20-28; claims 10-12). Succinamide is represented by the following chemical structure:



Ethosuximide, the preferred succinamide in the '867 patent, is represented by the following chemical structure:



Unlike the '867 patent, the claimed invention is directed to zonisamide, which is represented by the following chemical structure:



As can be seen from a comparison of the above chemical structures, the claimed zonisamide is structurally unrelated to the compounds (e.g., succinamides) described in the '867 patent. One skilled in the art would not make any assumptions about the chemical activity or potential uses of zonisamide based on the unrelated chemical compounds taught in the '867

patent. The '867 patent is non-analogous art that describes compounds that are completely unrelated to the claimed zonisamide. In view of the fact that the '867 patent is non-analogous art to the claimed invention, the PTO has not established a *prima facie* case of obviousness.

Kito describes mechanisms of T-type calcium channel blockade by zonisamide and concludes (page 118):

[Zonisamide] inhibited T-type I_{Ca} in a concentration-dependent manner, and it enhanced steady-state inactivation. The blockade of T-type calcium channels by [zonisamide] could suppress an important component of the inward current that underlies epileptiform cellular bursting, thereby inhibiting the spread of seizure activity.

Kito does not disclose or suggest any relationship between zonisamide and tremors.

Applicant respectfully submits that the PTO has made an impossible leap in logic to assert that because succinamides, which depress transient calcium currents, are useful in treating tremors, then any compound known in the art that depresses transient calcium currents would also be useful in treating tremors – regardless of the chemical structure or other chemical properties of the compounds. There is no scientific basis for the PTO's assertion that all calcium channel blockers are useful for treating tremors.

Contrary to the assertions made by the PTO, Taira, *No To Shinkei*, 44(1):61-63 (1992)¹ teaches that zonisamide use in the treatment of epilepsy caused two patients to develop side effects of resting and postural hand tremor. This reference would lead one skilled in the art to conclude (i) that zonisamide would not be useful for treating tremors and (ii) that every compound that exhibits calcium channel inhibition would not be useful for treating tremors. The teachings in this reference contradict the PTO's rejection.

One skilled in the art would not reasonably expect zonisamide to be useful in treating tremors based on a combination of the '867 patent and Kito. Accordingly, one skilled in the art would not be motivated by the combination of cited references to arrive at the claimed invention. Knowing one particular mechanism of action for one class of compounds (e.g., succinamides) is not reasonably sufficient to predict whether all compounds having that mechanism of action

¹ A copy of the Abstract of this Japanese-language document is submitted in the Information Disclosure Statement concurrently herewith.

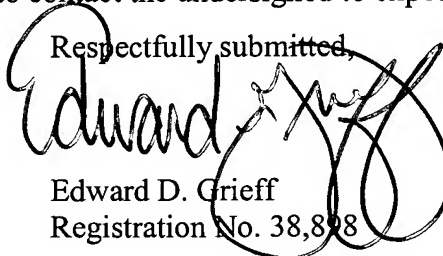
(e.g., regardless of the level thereof) would be useful in treating the same diseases (e.g., tremors). There is no scientific basis for the PTO's assertion that each and every compound that exhibits any level of calcium channel inhibition would be useful in treating tremors.

Furthermore, Applicant respectfully disagrees that one of ordinary skill would have been motivated to employ another therapeutic agent, in addition to zonisamide, in a method of treating action tremor. *In re Kerkhoven* is cited by the examiner for the proposition that it would be obvious to combine two compounds known to treat tremor individually to form a third compound for treating the same disorder. However, the Kerkhoven court stated that the idea of combining the two compounds must flow logically from them having been individually taught in the prior art.² The Examiner has not cited any prior art disclosing or even suggesting that zonisamide is useful for treating tremors. Instead, the Examiner impermissibly relies on Applicant's own disclosure for this teaching.

Applicant respectfully submits that the '867 patent in view of Kito does not render the pending claims obvious, and respectfully requests that the rejection under 35 USC § 103 be withdrawn.

Conclusion

An early and favorable consideration and allowance of claims 12-35 is respectfully requested. The Examiner is encouraged to contact the undersigned to expedite prosecution.

Respectfully submitted,

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² *In re Kerkhoven*, 205 USPQ at 11.